REMARKS

Reconsideration of this application is respectfully requested. New claims 70-72 have been added. Support for these claims is found in the original specification at, e.g., pages 11-13 (Examples 5 and 6). No new matter has been added. Claims 37-72 are pending and at issue.

Indefiniteness Rejection

Claims 37-69 have been rejected as indefinite for reciting that the composition comprises *Mycobacterium w* in "sonicated" or "solvent extract" form. The Examiner states that there are no method steps recited for obtaining the various solvent extracts, and that the components of the extracts would be expected to vary based on the method steps used. According to the Examiner, it is unclear if all extracts of *Mycobacterium w* would possess therapeutic properties.

The rejection is respectfully traversed.

Applicants respectfully submit that the pending claims are not indefinite because the scope of "sonicated" or "solvent extracts" of *Mycobacterium w* would have been readily understood by the skilled person. The term "solvent extract" is known in the art to refer to the separation of materials of different chemical types and solubilities by selective solvent action. In other words, a solvent extract of *Mycobacterium w* covers components selectively dissolved in solution when *Mycobacterium w* is treated with the specific solvents recited in the claim. The claims specifically recite that the solvent extraction is performed using one of a few organic solvents: chloroform, ethanol, methanol, acetone, phenol, isopropyl alcohol, acetic acid, urea, or hexane. *See* specification at, e.g., page 10. The specification further describes exemplary compositions of

solvent extracts prepared with 1 x 10^{10} *Mycobacterium w* cells treated with either methanol, chloroform, acetone or ethanol. *See* specification at, e.g., pages 6 and 7.

The term "sonication" is known by those of ordinary skill to refer to sound-induced agitation of particles in a sample. The skilled artisan would therefore understand that "sonicated" *Mycobacterium w* represent a sound-agitated sample of *Mycobacterium w*.

In view of the foregoing, applicants respectfully submit that the claims are definite, and request withdrawal of this rejection.

Enablement Rejection

Claims 37-69 have been rejected for lacking enablement. The Examiner contends that the specific dosage administered, the route of administration, and frequency of administration are not provided, and that it is unclear whether *Mycobacterium w* is present in whole cell, disrupted cell, or fractionated cell form. The Examiner further argues that the results in the specification are anecdotal only.

The rejection is traversed and reconsideration is respectfully requested.

The claims recite that the *Mycobacterium w* is present in the compositions in heat killed whole cell, sonicated, solvent extract, or enzyme extract form. Thus the claims specify the particular form of the *Mycobacterium w*. The specification also describes how to obtain each specific form of *Mycobacterium w*. Methods for culturing, harvesting, and sterilizing *Mycobacterium w* cells can be achieved according to the detailed protocols provided in the specification at, e.g., pages 7-9. Heat killed whole cell *Mycobacterium w* can then be obtained by treating the harvested *Mycobacterium w* cells with heat or ionizing radiation. Heat can be in the

form of, e.g., dry heat, moist heat, boiling or pasteurization. Ionizing radiation can include, e.g., ultraviolet, gamma ray, or microwave radiation. *See* specification at page 9. The harvested *Mycobacterium w* cells can be disrupted by way of sonication to form the sonicated *Mycobacterium w* samples. *See* specification at page 10. Solvent extract forms of *Mycobacterium w* can be obtained using organic solvents such as chloroform, ethanol, methanol, acetone, phenol, isopropyl alcohol, acetic acid, urea, or hexane. *See* specification at page 10. The specification also discloses that the enzyme extract form of *Mycobacterium w* can be obtained, e.g., by treating harvested *Mycobacterium w* cells with proteolytic enzymes such as liticase and pronase which digest cell wall/membranes. *See* specification at page 10.

The specification further provides significant guidance with respect to the dosage amounts. For instance, the specification provides exemplary 0.1 mL dosage compositions comprising *Mycobacterium w* in heat killed whole cell, sonicated, solvent extract, or enzyme extract form. *See* Example 1 (p. 5-7) of the specification. Heat killed whole cell *Mycobacterium w* is used in compositions A-C at cell counts of 0.5×10^9. The 0.1 mL dosage described for composition D contains $1x10^{10}$ sonicated *Mycobacterium w* cells. Solvent extract compositions E-H are disclosed to contain $1x10^{10}$ *Mycobacterium w* cells treated with either methanol, chloroform, or acetone. Composition I recites that the 0.1 mL dosage contains a liticase extract of $1x10^{10}$ *Mycobacterium w* cells.

The route of administration and frequency of administration of the dosage forms are also clearly exemplified in the specification. *See* the specification at, e.g., pages 5-7 and 10-14. The specification suggests that the 10 exemplary compositions recited on pages 5-7 are for "injection

I.P" administration. *See*, for instance, composition A on p. 5 which includes "Water for Injection I.P."

In the clinical study described in Example 4, Case 1, a 0.1 mL dose was administered intradermally over the deltoid region at a frequency of once a week for three months. *See* the specification at page 11, lines 10-21. Example 5 teaches that a 0.1 mL dose administered intradermally at a frequency of once a month for two months is effective. *See* the specification at page 12, lines 12-27. Five patients with muscle invasive bladder cancer were effectively treated in the study described in Example 6 upon monthly intradermal deltoid injection of a 0.1 mL dose of *Mycobacterium w* for six months. *See* specification at pages 12-13. Example 8(a) discloses that the 0.1 mL *Mycobacterium w* dosage can be administered by intradermal injection one a week for two months followed by every 15 days for two months and monthly for two months for a duration of six months for effective treatment. The 0.1 mL Mycobacterium w dosage was administered intradermally over the deltoid region every 15 days for three months in Example 8(b). *See* specification at pages 13-14. Thus, the specification provides extensive disclosure relating to route and frequency of administration of *Mycobacterium w*.

Further, there are well established techniques for determining an effective dose and route and frequency of administration. Accordingly, one of ordinary skill in the art could determine proper dosage amounts and routes and frequency of administration of the claimed compositions without undue experimentation.

Applicants respectfully submit that the Examiner's assertion that the present specification only provides "anecdotal evidence" that the claimed compositions are an effective means for treating cancer is incorrect. Further, as discussed below, such an assertion is irrelevant to the

present determination of enablement under 35 U.S.C.§112, first paragraph. The specification provides nine human clinical trials which demonstrate the effective use of *Mycobacterim w* for treatment of a variety of cancer types. The clinical trials described in the specification were conducted with a set of controls that demonstrate that the results correlate directly with the presence of the *Mycobacterium w* composition. Two of the controlled studies involved a large sample size of 20 patients. *See* the specification at, e.g., pages 11-14.

The Examiner appears to require highly extensive human testing to satisfy enablement, but this is not the proper standard under §112, first paragraph. MPEP §2164.02 states:

> [L]ack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement. A single working example in the specification for a claimed invention is enough to preclude a rejection which states that nothing is enabled since at least that embodiment would be enabled.

MPEP §2164.02, quoting *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987), further states:

> An applicant need not have actually reduced the invention to practice prior to filing … "The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." 822 F.2d at 1078, 3 USPQ2d at 1304 (quoting *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325 (CCPA 1956)). The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

Thus, the human clinical trials disclosed in the specification go above and beyond the requirements for enablement under 35 U.S.C. §112, first paragraph.

In view of the foregoing, one of ordinary skill in the art would be able to make and use the invention recited in claims 37-69 without undue experimentation. Accordingly, claims 37-69 are fully enabled, and Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered, and that the pending claims be allowed and the case passed to issue.

If there are any other issues remaining that the Examiner believes can be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

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By /Jay P. Lessler/
Jay P. Lessler
Registration No.: 41,151
DARBY & DARBY P.C.
P.O. Box 770
Church Street Station
New York, New York 10008-0770
(212) 527-7700
(212) 527-7701 (Fax)
Attorneys/Agents For Applicant